Amendments to the Claims

I. Amendments

Please withdraw claims 16-46, as directed to non-elected inventions without prejudice or disclaimer with respect to the claimed subject matter.

II. The Claims of the Application

Claim 1. **[Original]** A method of producing a folded extramembranous receptor domain of a membrane protein receptor. said method comprising:

forming a chemical ligation product comprising an extramembranous receptor domain of a selected membrane protein receptor by ligating under chemoselective chemical ligation conditions first and second peptides of said extramembranous receptor domain. said peptides having compatible unprotected chemoselective reactive groups capable of forming a covalent bond therein between;

exposing said chemical ligation product to a folding buffer having a buffering reagent, a chaotropic reagent and an organic solvent that mimics the water-lipid interface environment of a cell membrane; and

isolating from said folding buffer chemical ligation product that binds to a ligand of said extramembranous receptor domain of said membrane protein receptor, whereby a folded extramembranous receptor domain of a membrane protein receptor is produced.

Claim 2. **[Original]** The method of Claim 1 wherein said extramembranous receptor domain is an extracellular domain.

Claim 3. **[Original]** The method of Claim 2 wherein said extracellular domain is an amino terminal domain.

Claim 4. **[Original]** The method of Claim 2 wherein said extramembranous receptor domain is derived from a receptor selected from the group consisting of a G-protein coupled receptor and an enzyme-linked protein receptor.

Claim 5. **[Original]** The method of Claim 4 wherein said G-protein coupled receptor is a type B G-protein coupled receptor.

Claim 6. **[Original]** The method of Claim 5 wherein said type B G-protein coupled receptor is glucagon-like peptide 1 receptor.

Claim 7. **[Original]** The method of Claim 1 wherein said chemical ligation is selected from the group consisting of native chemical ligation, oxime-forming ligation, thioester-forming ligation, thioether-forming ligation, hydrazone-forming ligation, thiazolidine-forming ligation, and oxazolidine-forming ligation.

Claim 8. **[Original]** The method of Claim 1 wherein said organic solvent is a water soluble organic solvent.

Claim 9. **[Original]** The method of Claim 8 wherein said water soluble organic solvent is methanol.

Claim 10. **[Original]** The method of Claim 1 wherein said first peptide comprises an unnatural amino acid.

Claim 11. **[Original]** The method of Claim 10 wherein said unnatural amino acid comprises a chemical moiety selected from the group consisting of a chromophore and a hapten.

Claim 12. **[Original]** The method of Claim 11 wherein said chromophore is a fluorophore.

Claim 13. **[Original]** The method of Claim 11 wherein said hapten comprises a biotin moiety.

Claim 14. **[Original]** A composition comprising a chemically synthesized extramembranous receptor domain produced according to the method of Claim 1.

Claim 15. **[Original]** A kit comprising a composition according to Claim 14.

Claim 16. **[Withdrawn]** A composition comprising a synthetic extramembranous receptor domain of a membrane protein receptor having a chemically synthesized segment that includes an unnatural amino acid at a pre-selected residue position, wherein said extramembranous receptor domain is free of a membrane spanning transmembrane domain and is capable of binding to a ligand of said membrane protein receptor.

Claim 17. **[Withdrawn]** The composition of Claim 16 wherein said composition is completely free of cellular contaminants.

Claim 18. **[Withdrawn]** The composition of Claim 16 wherein said unnatural amino acid comprises a chemical moiety selected from the group consisting of a chromophore and a hapten.

Claim 19. **[Withdrawn]** The composition of Claim 18 wherein said chromophore is a fluorophore.

Claim 20. **[Withdrawn]** The composition of Claim 18 wherein said hapten comprises a biotin moiety.

Claim 21. **[Withdrawn]** The composition of Claim 16 wherein said synthetic extramembranous receptor domain is attached to a support matrix.

Claim 22. **[Withdrawn]** The composition of Claim 21 wherein said support matrix is a MALDI slide.

Claim 23. **[Withdrawn]** The composition of Claim 21 wherein said support matrix is a polymer.

Claim 24. **[Withdrawn]** A method of assaying a soluble extramembranous receptor domain for ligand-induced dimerization, said method comprising:

contacting a soluble extramembranous receptor domain of a membrane protein receptor with a ligand of said membrane protein, wherein said soluble extramembranous receptor domain is free of a membrane spanning transmembrane domain; and

assaying said soluble extramembranous receptor domain for ligand-induced dimerization.

Claim 25. **[Withdrawn]** The method of Claim 24 wherein said soluble extramembranous receptor domain comprises an unnatural amino acid.

Claim 26. **[Withdrawn]** The method of Claim 25 wherein said unnatural amino acid comprises a chemical moiety selected from the group consisting of a chromophore and a hapten.

Claim 27. **[Withdrawn]** The method of Claim 26 wherein said chromophore is a fluorophore.

Claim 28. **[Withdrawn]** The method of Claim 26 wherein said hapten comprises a biotin moiety.

Claim 29. **[Withdrawn]** The method of Claim 24 wherein said extramembranous receptor domain is attached to a support matrix.

Claim 30. **[Withdrawn]** The method of Claim 25 wherein said assaying is characterized by detection of a property of said unnatural amino acid.

Claim 31. **[Withdrawn]** The method of Claim 30 wherein said unnatural amino acid comprises a chromophore and said property is fluorescence.

Claim 32. **[Withdrawn]** The method of Claim 24 wherein said ligand comprises a detectable label.

Claim 33. **[Withdrawn]** The method of Claim 32 wherein said detectable label is a chromophore.

Claim 34. **[Withdrawn]** The method of Claim 24 wherein said assaying is characterized by detection of a property of said ligand.

Claim 35. **[Withdrawn]** The method of Claim 34 wherein said ligand comprises a chromophore and said property is fluorescence.

Claim 36. **[Withdrawn]** A method of detecting binding of a ligand to an extramembranous receptor domain of a membrane protein receptor, said method comprising:

contacting a soluble extramembranous receptor domain of a membrane protein receptor with a ligand of said membrane protein receptor, wherein said soluble extramembranous receptor domain is free of a membrane spanning transmembrane domain and comprises an unnatural amino acid having a detectable moiety; and

assaying said soluble extramembranous receptor domain for ligand-induced dimerization of monomers of said extramembranous receptor domain.

Claim 37. **[Withdrawn]** The method of Claim 36 wherein said ligand is selected from the group consisting of agonist and antagonist.

Claim 38 **[Withdrawn]** The method of Claim 37 wherein said antagonist is a partial antagonist.

Claim 39. **[Withdrawn]** The method of Claim 37 wherein said agonist is a partial agonist.

Claim 40. **[Withdrawn]** The method of Claim 36 wherein said extramembranous receptor domain is an extracellular domain.

Claim 41. **[Withdrawn]** A method of detecting binding of a ligand to an extramembranous receptor domain of a membrane protein receptor, said method comprising:

contacting a soluble extramembranous receptor domain of a membrane protein receptor with a ligand for said membrane protein receptor, wherein said soluble extramembranous receptor domain is free of a membrane spanning transmembrane domain and comprises an unnatural amino acid having a detectable moiety; and

detecting binding of said ligand to said soluble extramembranous receptor domain by assaying for a change in a property of said detectable moiety.

Claim 42. **[Withdrawn]** The method of Claim 41 wherein said detectable moiety is a chromophore and said property is energy transfer.

Claim 43. **[Withdrawn]** The method of Claim 41 wherein said ligand is selected from the group consisting of agonist and antagonist.

Claim 44. **[Withdrawn]** The method of Claim 43 wherein said antagonist is a partial antagonist.

Claim 45. **[Withdrawn]** The method of Claim 43 wherein said agonist is a partial agonist.

Claim 46. **[Withdrawn]** The method of Claim 41 wherein said soluble extramembranous receptor domain is an extracellular domain.